

PATENT  
DIVER1240-3

Applicant:  
Warren and Swanson  
Application No.: 09/389,537  
Filed: September 2, 1999  
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## II. REMARKS

These remarks are in response to the Office Action mailed July 3, 2001. Applicants

submit that the amendments to the claims are for clarity and should not be construed as amendments affecting patentability under *Festo Corp. v. Shoketsu Kinzoku Kogyo Kabushiki Co.*, 234 F.3d 558, 56 USPQ2d 1865 (Fed. Cir. 2000) (en banc). Additionally, new claims 28 and 29 have been added. As drafted, these claims are fully supported by the specification, as filed, and do not add new matter. Thus, upon entry of the amendment, claims 17-29 are under examination.

## A. OBJECTION TO THE SPECIFICATION

The specification of the present application was objected to due to the following informalities, as set forth in Paper No. 12: the ATCC number, for example, on pages 3 and 6, is not specified, there is no description of Figures 9 and 10, the description of Figure 11 is incorrect, the specification incorporates expired provisional application 60/008,316 by reference, the specification does not contain sequence identifiers in all instances where the specification discusses sequences, and the paper copy and electronic copies of the Sequence Listing are different. As these objections have been remedied by the amendments of the present Response, it is respectfully requested that the above objections be withdrawn.

It is respectfully submitted that the reference to the ATCC number on pages 3 and 6 has been removed, as set forth above. As the language is no longer present in the specification, it is respectfully submitted that the objection is moot.

As the amendments set forth above provide accurate descriptions of Figures 9, 10 and 11, it is respectfully requested that the objection to these figures be withdrawn.

The specification is objected to in that expired provisional application 60/008,316 is incorporated by reference. It is respectfully submitted that an application was filed, claiming priority to provisional application 60/008,316 prior to expiration of the provisional application.

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Applicants respectfully traverse the rejection of claims 17 to 27 under 35 U.S.C. § 112, first paragraph, for containing subject matter allegedly not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession

# **B. REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH**

§ 1.821-1.825. Applicants respectfully traverse the rejection of claims 17 to 27 under 35 U.S.C. § 112, first paragraph, for containing subject matter allegedly not described in the Specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the computer readable form of the sequence listing. In view of the above, Applicants believe that the application now complies with the requirements for sequences under 37 C.F.R. Accordingly, Applicants respectfully request entry of the substitute paper copy and the substitute Submitted concurrently is an executed statement under 37 C.F.R. § 1.825(b) to that effect. of the computer readable form and does not include new matter to the as-filed application. and a clean paper copy of the same. The substitute paper copy is identical to the substitute copy a substitute copy of the computer readable form of the sequence listing of the present application paper copy and electronic copies of the Sequence Listing are different, Applicants are submitting Use Sequence Listing" filed January 19, 2001. However, in response to the objection that the form thereof were submitted in the above-referenced application by virtue of the "Permission to § 1.821-1.825. It is respectfully submitted that the Sequence Listing and computer readable requirements for applications having nucleotide and/or amino acid sequences under 37 C.F.R. The application is also objected to in that the application fails to comply with the

identifiers. It is therefore respectfully requested that the objection be withdrawn. amendments made to the last two paragraphs on page 27, remedy the lack of sequence instances. It is respectfully submitted that the amendments to the specification, particularly those The specification is also objected to, in that sequence identifiers are not used in all application. As such, it is respectfully requested that the objection be withdrawn

therefore respectfully submitted that this amendment remedies the incorporation of an expired Patent Number claiming priority to Provisional Application Serial Number 60/008,316. It is The amendment to the specification above has incorporated the serial number of the new U.S.

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of the invention at the time of filing of the Application. In particular, it is alleged in Paper No. 12 that claims 17 to 27 are directed to a vast diverse class of enzymes with structural limitations, but no specific functional limitations. (Paper No. 12, page 4).

Applicants respectfully disagree. It is alleged in the Paper No. 12 that "[t]he claims are not drawn to an aspartate transaminase having an amino acid sequence that is 70% identical to SEQ ID NO:25 for example, but to any transaminase or aminotransferase." (Paper No. 12, page 8.) Applicants respectfully submit that the claims, as pending, include both structural and functional requirements for the claimed enzyme. Structurally, the claimed enzyme must be at least 70% identical to any one of SEQ ID NOS: 25-32. Functionally, the claimed enzyme must have transaminase or aminotransferase activity. If an enzyme does not possess both of these characteristics, it falls outside of the claim. The claims are not drawn to any transaminase or aminotransferase, as alleged in Paper No. 12, but to an enzyme that is at least 70% identical to any one of SEQ ID NOS: 25-32 and has transaminase or aminotransferase activity. As such, an enzyme of the claimed invention discloses sufficient identifying characteristics to allow one of skill in the art to distinguish a transaminase or aminotransferase of the invention from a transaminase or aminotransferase that does not fall within the scope of the claims. It is respectfully submitted that claims 17, 18 and claims dependent therefrom meet the written description requirement of 35 U.S.C. §112, first paragraph. Accordingly, the removal of the rejection is requested.

Additionally, the Examiner's attention is drawn to new claims 28 and 29 where claims 17 and 18, respectively, are further defined. Claims 28 and 29 specify that the enzyme claimed in claim 17 and used in the method of claim 18 have the same amino group acceptor and amino group donor as the enzyme to which it is at least 70% identical. Therefore the claims provide clarification of the structural and functional limitations of the enzyme in claims 17 and 18, in order to distinguish the claimed enzymes from all other enzymes or proteins.

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Similarly, Applicants respectfully traverse the rejection of claims 17 to 27 under 35 U.S.C. § 112, first paragraph, for allegedly being non-enabled for a transaminase or aminotransferase having an amino acid sequence 70%, 80%, 90% or 95% identical to SEQ ID NOS: 25-32 and a method of use thereof.

Applicants respectfully draw the Examiner's attention to claims 17 and 18. As set forth above, these claims contain both structural and functional characteristics of the claimed enzyme. One of skill in the art would therefore be able to make and use the claimed invention without any undue burden. Even where there are multiple transaminase or aminotransferase activities, one of skill in the art would have known, at the time of filing of the application, how to determine whether an enzyme with at least 70% homology to any one of SEQ ID NOS: 25-32 has

transaminase or aminotransferase activity or whether the enzyme does not have transaminase or aminotransferase activity. Therefore, claims 17, 18 and claims dependent therefrom meet the enablement requirement of 35 U.S.C. § 112, first paragraph. Accordingly, the removal of the rejection is requested.

**C. REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH**

Applicants respectfully traverse the rejection of claims 17 to 27 under 35 U.S.C. § 112, second paragraph, as allegedly indefinite for failing to point out and distinctly claim the subject matter which Applicant regards as the invention. Applicants respectfully traverse the rejection. Specifically, claims 17 and 18 are rejected for recitation of "the amino acid sequence set forth in SEQ ID NOS: 25-32." In accordance with the Examiner's suggestion, claims 17 and 18 have been amended to recite "any one of SEQ ID NOS: 25-32." As such, it is respectfully requested that the rejection be removed.

Similarly, claim 18 has been rejected for recitation of "an enzyme which is at least 70% identical to the amino acid sequence." In order to clarify the claim, the claim has been amended

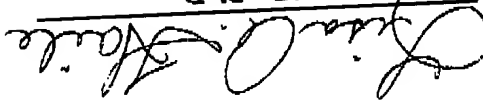
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Lisa A. Haile, J.D., Ph.D.  
Reg. No. 38,347  
Telephone: (858) 677-1456  
Facsimile: (858) 677-1465

Date: December 3, 2001



Respectfully submitted,

If the Examiner would like to discuss any of the issues raised in the Office Action, Applicant's representative can be reached at (858) 677-1456. Please charge any additional fees, or make any credits, to Deposit Account No. 50-1355.

In summary, for the reasons set forth herein, Applicants maintain that claims 17 to 29 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

### CONCLUSION

Claims 23 to 27 are rejected as confusing, as claims 23 to 27 refer to an enzyme of claim 18, where claim 18 is drawn to a method. The preamble of claims 23 to 27 has been amended to recite "The method of claim 18." As such, it is respectfully submitted that claims 23 to 27 are not confusing, as amended, and it is respectfully requested that the rejection be removed.

to recite "an enzyme encoded by an amino acid sequence which is at least 70% identical to the amino acid sequence." As such, it is respectfully requested that the rejection be removed.

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# VERSION WITH MARKINGS TO SHOW CHANGES MADE

## In the specification:

On page 3:

In accordance with another aspect of the present invention there are provided isolated nucleic acid molecules encoding mature polypeptides expressed by the DNA [contained in ATCC Deposit No. \_\_\_\_\_] encoding an enzyme of the present invention.

On page 5:

[Figure 9 is a diagrammatic illustration of the assay used to assess aminotransferase activity of the proteins using glutamate dehydrogenase.] Figure 9 shows the full-length DNA (SEQ ID NO.: 35) and corresponding deduced amino acid sequence (SEQ ID NO.: 36) of *Ammonifex degensii* histidinol phosphate aminotransferase. Figure 10 shows the full-length DNA (SEQ ID NO.: 39) and corresponding deduced amino acid sequence (SEQ ID NO.: 40) of *Aquifex aspartate* aminotransferase. Figure 11 is a diagram of the assay used to assess aminotransferase activity of the proteins using glutamate dehydrogenase.

On page 6:

In accordance with another aspect of the present invention, there are provided isolated polynucleotides encoding the enzymes of the present invention. The deposited material is a mixture of genomic clones comprising DNA encoding an enzyme of the present invention. Each genomic clone comprising the respective DNA has been inserted into a PQB vector (Quiagen, Inc., Chatsworth, CA). [The deposit has been deposited with the American Type Culture Collection, 12301 Parklawn Drive, Rockville, Maryland 20852, USA, on December 13, 1995 and assigned ATCC Deposit No. \_\_\_\_\_.]

On page 22:

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Transaminases are highly stereoselective, and most use L-amino acids as substrates.

Using the approach disclosed in [a] commonly assigned U.S. Patent Number 5,939,250 [co-pending provisional application Serial No. 60/008,316, filed on December 7, 1995], filed on December 7, 1996 and entitled "Combinatorial Enzyme Development," the disclosure of which is incorporated herein by reference in its entirety, one can convert the transaminases of the invention to use D-amino acids as substrates. Such conversion makes possible a broader array of transaminase applications. For instance, D-valine can be used in the manufacture of synthetic pyrethroids. D-phenylglycine and its derivatives can be useful as components of  $\beta$ -lactam antibiotics. Further the thermostable transaminases have superior stability at higher temperatures and in organic solvents. Thus, they are better suited to utilize either L- and/or D-amino acids for production of optically pure chiral compounds used in pharmaceutical, agricultural, and other chemical manufactures.

On page 27:

*Ammonifex degensii* bp aminotransferase

5'-CCGAGAAATTCATTAAAGAGGAGAAATTAACTATGGCAGTCAAGTGGCGGCT

(SEQ ID NO: 33)

3'-CGGAGGATCCTTATCCAAAGCTTCCAGGAAG (SEQ ID NO: 34)

Homology information:

Closest to *Bacillus subtilis* (reference: Henner, D.J., Band, Flags G., Chen E., Gene 49:147-152(1886). Percent similarity:65.084 Percent identity 44.134

On page 27:

*Amylifer* aspartate aminotransferase

5'-CCGAGAAATTCATTAAAGAGGAGAAATTAACTATGAGAAAGGAGCTTGCAAGT

(SEQ ID NO: 37)

3'-CGGAGGATCCTTAGATCTCTCAAGGGCTTT (SEQ ID NO: 38)

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Closest to *Bacillus subtilis* (Sorkin, A.V., Azevedo, V., Zumbstein, E., Galleron, N., Ehrlich, S.D. and Serror, P. Determination and analysis of the nucleotide sequence of the *Bacillus subtilis* chromosome region between *serA* and *kds* loci cloned in yeast artificial chromosome Unpublished (1995). Percent similarity: 71.611 Percent identity: 52.685

# In the claims:

17. (Amended) An isolated enzyme [comprising a member selected from the group consisting of an enzyme] comprising an amino acid sequence which is at least 70% identical to [the amino acid sequence set forth in] any one of SEQ ID NOS:25-32 when aligned using the BLASTN program of the National Center for Biotechnology Information, wherein the enzyme has [activity as a] transaminase or aminotransferase activity.

18. (Amended) A method for transferring an amino group from an amino acid to an  $\alpha$ -keto acid comprising:

contacting an amino acid in the presence of an  $\alpha$ -keto acid with an isolated enzyme selected from the group consisting of an enzyme encoded by an amino acid sequence which is at least 70% identical to [the amino acid sequence set forth in] any one of SEQ ID NOS: 25-32 when aligned using the BLASTN program of the National Center for Biotechnology Information wherein the enzyme has transaminase or aminotransferase activity; and

thereby transferring an amino group from the amino acid to the  $\alpha$ -keto acid.

19. (Amended) An enzyme of claim 17, wherein the amino acid sequence of the isolated enzyme is at least 80% identical.

20. (Amended) An enzyme of claim 17, wherein the amino acid sequence of the isolated enzyme is at least 90% identical.

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21. (Amended) An enzyme of claim 17, wherein the amino acid sequence of the isolated enzyme is at least 95% identical.

22. (Amended) An enzyme of claim 21, wherein the isolated enzyme is microbial.

23. (Amended) [An enzyme] The method of claim 18, wherein the amino acid sequence of the isolated enzyme is at least 80% identical.

24. (Amended) [An enzyme] The method of claim 18, wherein the amino acid sequence of the isolated enzyme is at least 90% identical.

25. (Amended) [An enzyme] The method of claim 18, wherein the amino acid sequence of the isolated enzyme is at least 95% identical.

26. (Amended) [An enzyme] The method of claim 25, wherein the isolated enzyme is microbial.

27. (Amended) [An enzyme] The method of claim 25, wherein the isolated enzyme converts about 400  $\mu$ moles of  $\alpha$ -keto acid per minute per mg of the enzyme.

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Attorney Docket No.: DIVER1240-3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Warren and Swanson  
 Serial No.: 09/389,537  
 Filed: September 2, 1999  
 Title: TRANSAMINASES AND AMINOTRANSFERASES  
 Examiner: Slobodyansky B.  
 Art Unit: 1652

Commissioner for Patents  
 Washington, D.C. 20231

VERIFIED STATEMENT UNDER 37 C.F.R. § 1.821(d)

Sir:

I, Mikhail Bayley, declare that I personally prepared the paper and the computer-readable copies of the Sequence Listing herewith in the above-entitled case and that the content of both is the same.

I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of The United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 11/30/2001  
 GRAY CARY WARB & FRIEDENRICH LLP  
 4365 Executive Drive, Suite 1100  
 San Diego, CA 92121-2133

Customer Number: 28213

CERTIFICATION UNDER 37 CFR §1.8	
I hereby certify that the documents referred to as enclosed herein are being deposited with the United States Postal Service as first class mail on this date, December 3, 2001, in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231.	
Aldon Griffiths	
Name of Person Mailing Paper	
Signature	
December 3, 2001	Date

Attorney Docket No.: DIVER1240-3

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Warren and Swanson  
 Serial No.: 09/389,537  
 Filed: September 2, 1999  
 Title: TRANSAMINASES AND AMINOTRANSFERASES  
 Examiner: Slobodyansky B.  
 Art Unit: 1652

Commissioner for Patents  
 Washington, D.C. 20231

STATEMENT UNDER 37 C.F.R. §§ 1.821(d) and (e)

Sir:

I hereby state, as required by 37 C.F.R. § 1.821(f), that the information recorded in computer readable form is identical to the written sequence listing.  
 I hereby state that the submission, filed in accordance with 37 C.F.R. § 1.821 (g), herein does not include new matter.

Respectfully submitted,

*Lisa A. Haile*  
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Customer Number: 28213

Date: December 3, 2001

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Aldon Griffiths	
Name of Person Mailing Paper	
Signature	
Date	December 3, 2001

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<110> DIVERSA CORPORATION  
WARREN, Patrick  
SWANSON, Ronald

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 tctaagtact tctgtatgcc aggtttcagg atagggtgga tgatagtcc ggaagaactc 720  
 gtgagaaagg cggaaatagt aattcagaac gtatttatat ctgcccagac gctcagtcag 780  
 tacgcgcgcc ttgaggcttt tgattacgag tatttgagaa aggttaagaaa aacctttgaa 840  
 gagaggagga acttccttta tggggaaactg aaaaaactct tcaagataga cgcgaaacct 900  
 caggagagctt ttacgtatg ggcaaacata agtgattact ccacagatag ctacgaattt 960  
 gctttaaaac ttttaaggga ggcgagggtg gcggtaacgc ccggggtgga ctttgaaaaa 1020  
 aacaaaacga aggagtatat aaggtttgc tatacgagaa agatagaaga acttaaggag 1080



ggcgttgaaa ggataaagaa gttcttagag aagcttagct ga

1122

&lt;210&gt; 19

&lt;211&gt; 1362

&lt;212&gt; DNA

&lt;213&gt; Aquifex

&lt;400&gt; 19

atgtgggaat tagacctaa aacgctcgaa aagtgggaca aggagtactt ctggcatcca 60

tttaccacaga tgaaggtcta cagagaagaa gaaaacctga tatttgaacg cggagaaggc 120

gtttacctgt gggacatata cggcaggaag tatatagatg ccatactctt cctctggtgc 180

aacgtccacg gacataacca ccctaactg aacacgcgag ttatgaaaca gctctgtaag 240

gtagctcaca caactactct gggaagttcc aacgttcccg ccatactcct tgcaaagaag 300

cttgtagaaa tttctcctga aggattaaac aaggtctttt actccgaaga cgggtgcggaa 360

gcagtagaga tagcgataaa gatggcttat cactactgga agaacaaggg agttaagggg 420

aaaaacgttt tcataacgct ttccgaagcc taccacgggg atactgtagg agcgggttagc 480

gtagggggta tagaactcct ccacgggaact tataaagatc tccttttcaa gactataaaa 540

ctcccatctc cttaacctga ctgcaaggaa aagtacgggg aactctgcc tgagtgcacg 600

gcagatttat taaaacaact ggaagatatc ctgaagtcgc gggaagatat cgttgcggtc 660

attatggaag cgggaattca ggcagccgcg ggaatgctcc ccttccctcc gggatttttg 720

aaaggcgtaa gggagcttac gaagaatac gacactttaa tgatagttga cgagggttgc 780

acgggatttg gcaggacggg aacgatgttt tactgtgagc aggaaggagt cagtccggac 840

tttatgtgtc taggttaaggg tataaccgga gggtagctcc cgcttgctgc gacactcaca 900

acggacgagg tgttcaatgc ctttttaggt gagttcgggg aggdaagca cttttaccac 960

gggcacacct acaactgaaa taacctcgcc tgttcggtg cactcgcaaa cttagaagtt 1020

tttgaggaag aaagaacttt agagaagctc caaccaaaga taaagctttt aaaggaaagg 1080

cttcaggagt tctgggaact caagcacgtt ggagatgtta gacagctagg ttttatggct 1140

ggaatagagc tgggtgaaggc caaagaaaag ggagaacctt tccttaacgg tgaaaggacg 1200

ggatttaagg tggcttadac gtgcaggga aaaggggtgt ttttgagacc gctcggagac 1260

gttatggtat tgatgatgcc tcttgtaata gaggaagacg aaatgaacta cgttatattat 1320

acacttaaat gggcaattaa agagcttgaa aaagaggtgt ag 1362

&lt;210&gt; 20

&lt;211&gt; 1032

&lt;212&gt; DNA

&lt;213&gt; Aquifex

<400> 20  
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 gtttacctgt acgatgagga aggaaaggag tatcttgact ttgtctccgg tataggcgctc 120  
 aactccctcg gtcaacgotta cccaaaactc acagaagctc taaaagaaca ggttgagaaa 180  
 ctctccacg tttcaaactc ttacgaaaac ccgtggcagg aagaactggc tcacaaactt 240  
 gtaaaacact tctggacaga agggaaaggta tttttcgcaa acagcggaac ggaaagtgt 300  
 gagggcggtc taaagctcgc aaggaaagtac tggaggggata aaggaaagaa caagtggag 360  
 tttatatcct ttgaaaactc ttccacggg agaactacg gtagcctctc cgcaacggga 420  
 cagccaaagt tccacaaagg ctttgaaact ctagtctctg gattttctta cgcaagctg 480  
 aacgatatag acagcgttta caaactccta gacgaggaaa ccgcggggat aattattgaa 540  
 gttatacaag gagagggcgg agtaaacgag gcgagtgagg atttttotaag taaactccag 600  
 gaaatttgta aagaaaaaga tgtgtctotta attatagacg aagtgcacaa cgggaatagga 660  
 aggaccgggg aattctacgc atatcaadac ttcaactctaa aacoggacgt aattgcgctt 720  
 gcgaagggaac tcggaggagg tgtgccaata ggtgccatcc ttgcaaggga agaagtggcc 780  
 cagagcttta ctcccggtc ccacggctct accttcggag gaaacccctt agcctgcagg 840  
 gcgggaacag tggtagtaga tgaagttgaa aaactccctg ctacagtaag ggaagtgggg 900  
 aattacttca aagaaaaact gaaggaaactc ggcaaggga aggtaaaggg aagaggattg 960  
 atgctcggtc ttgaacttga aagagagtggt aaagattacg ttctcaaggc tcttgaaagg 1020  
 gaattctcat aa 1032

<210> 21  
 <211> 1197  
 <212> DNA  
 <213> *Ammonifex degensii*

<400> 21  
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 accaaggcca aggagctttt gcggcagggg gaaagggtca tcaatttcgg ggccggggag 120  
 ccggacttcg atacaccgga acacatcaag gaagcggcga agcagacttt agatcagggc 180  
 ttaaccaagt acacgccggt ggctgggata ttacctcttc gggaggccat atgcgagaag 240  
 ctttacccg acaatcaact ggaatacagc ccgaatgaga togtggtctc ctgtggcgcc 300  
 aagcattcta ttttcaacgc tctgcaggtc ctctggacc cgggggacga ggtgataatc 360  
 ccgtccctt actggacttc ctatccggag caggtgaagc tggcgggagg ggtgccggtt 420  
 ttcttccca cctctccga gaacgacttc aagctcaggc cgggaagatct acgtgcggct 480  
 gtaacccgc gcaccgcct ttgatctc aattcccgg ccaacccac aggcacogtt 540

taccgccggg aggaacttat cggcttagcg gaggtagccc tggaggccga cctatggatc 600  
 ttgtcggacg agatctacga aaagctgac tacgaacggga tggagcacgt gagcatagcc 660  
 ggcctcgacc cggagggtcaa aaagcgcacg attgtggtaa acggtgtttc caaggcttac 720  
 gccatgaccg gttggcgcat aggttatgct gccgctcccc ggccgatagc ccaggccatg 780  
 accaacctcc aaagccacag tacctctaac cccacttcgc tagcccaggc ggccggcgtg 840  
 gccgctctga agggggccaca agagccggtg gagaacatgc gccgggcttt tcaaaagcgg 900  
 cgggatttoa tctggcagta cctaaactcc ttaccgggag tgcgctgccc caaaccttta 960  
 ggggcctttt acgtcttttc agaagttgag cgggcttttg ggccgccgtc taaaaggacg 1020  
 ggaaatacta ccgctagcga cctggccctt ttctctctgg aagagataaa agtggccacc 1080  
 gtggctgggg ctgccttttg ggacgatcgc tacctgcgct ttctctacgc cctgoggtg 1140  
 gaagatatcg aagaggggat gcaacgggtt aaagaattga tcgaagcggc actttaa 1197

<210> 22  
 <211> 1779  
 <212> DNA  
 <213> Aquifex

<400> 22  
 atgtgcggga tagtcggata cgtagggagg gatttagccc ttcttatagt cctcggagct 60  
 cttgagagac tcgaatacag gggttacgac tccgcgggag ttgcccttat agaagacggg 120  
 aaactcatag ttgaaaagaa gaagggaag ataagggaac tcgttaaagc gctatgggga 180  
 aaggattaca aggctaaaac gggatataggc cacacacgct gggcaaccca cggaaagccc 240  
 acggacgaga acgcccaccc ccacaccgac gaaaaagggtg agtttgagc agttoacaac 300  
 gggataatag aaaactactt agaactaaaa gaggaactaa agaagggaag tgtaaagttc 360  
 aggtccgaaa cagacacaga agttatagcc caccctcatag cgaagaacta caggggggac 420  
 ttactggagg ccgtttttaa aaccgtaaag aaattaaagg gtgcttttgc ctttgcgggt 480  
 ataacgggtc acgaaccaa cagaactaata ggagtgaagc aggggagtc ttaatecgc 540  
 ggactcggag aaggagaaaa ctctctcgtc tcagatatc ccgcaatact tcttacacg 600  
 aaaaagatta ttgttcttga tgacggggaa atagcggacc tgactcccga cactgtgaac 660  
 atttacaact ttgagggaga gcccgtttca aagggaagtaa tgattaagcc ctgggatctt 720  
 gtttctgcgg aaaagggtgg ttttaaacac ttcatgctaa aagagatata cgaacagccc 780  
 aaagccataa acgacacact caagggtttc ctctcaaccg aagacgcaat accctttaag 840  
 ttaaaagact tcagaagggt tttaataata gcgtgogggg cctcttacca cgggggcttc 900  
 gtcggaaagt actggataga gagatttgca ggtgttccca cagaggtaat ttacgcttcg 960

gaattcaggt atgctggacgt tcccgtttcg gacaaggata tcgttatcgg aatttcccag 1020  
 tcaggagaga ccgctgacac aaagttrtgc ottcagtcgg caaaggaaaa gggagccttt 1080  
 accgtgggac tcgtaaacgt agtgggaagt gccatagaca gggagtcgga cttttccctt 1140  
 cacacacatg cgggacccga aataggcgtg ggggtacaa agaccttca cgcacagttc 1200  
 accgcactct acgcccttto ggtaaggga agtgaggaga gggaaaatct aataagactc 1260  
 cttgaaaagg ttccatcact cgttgaacaa acactgaaca ccgcagaaga agtggagaag 1320  
 gtagcggaaa agtacatgaa aaagaaaaac atgotttacc tcggaaggta cttaaattac 1380  
 cccatagcgc tggaggggagc tcttaaactt aaagaaattt cttacatata cgcggaagggt 1440  
 tatcccgtag gggagatgaa gcacgggtccc atagccctca tagacgaaaa catgccgggt 1500  
 gtggtaatcg caccgaaaga cagggtttac gagaagatac tctaaaacgt agaagaggtt 1560  
 ctgcgaagaa agggaaagggt tattttctgt ggcttttaag gagacgaaac tctcaaaagc 1620  
 aaatccgaga gcgttatgga aatccogaag gcagaagaac cgataactcc tttcttgacg 1680  
 gtaatacccc tgcaactctt tgctactctt atagcgagca aactgggact ggatgtggat 1740  
 cagccgagaa atctcgccaa aacgggtcac gtggaataa 1779

<210> 23  
 <211> 1065  
 <212> DNA  
 <213> Aquifex

<400> 23  
 atgatacccc agaggattaa ggaaottgaa gcttacaaga cggaggtoac tcccgcttcc 60  
 gtcaggcttt cctctaacga attcccttac gactttcccg aggagataaa acaaagggtcc 120  
 ttagaagaat taaaaaagggt tcccttgaac aaataccoag accccgaagc gaaagagtta 180  
 aaagcgggtc ttgcggattt tttcggcgtt aaggaaagaa atttagttct cggtaacggt 240  
 tcggacgaac tcataatacta cctctcaata gctatagggtg aactttacat acccgtttac 300  
 ataactgttc ccaccttttc catgtacgag ataagtgcga aagttctcgg aagacccctc 360  
 gtaaagggtc aactggacga aaactttgat atagacttag aaagaagtat tgaattaata 420  
 gagaaagaaa aaccggttct cgggtacttt gcttaaccaa acaaccctac gggaaacctc 480  
 ttttcagggg gaaagattga ggagataaga aacaggggtg tttctgtgt aatagacgaa 540  
 gcctactatc attactcggg agaaaccttt ctggaagacg cgtcaaaag ggaagatacg 600  
 gtagttttga ggacaotttc aaaaatcgggt atggcgagtt taagggtagg gattttaata 660  
 gggaaagggg aaatcgtctc agaaattaac aagggtgagac tcccttcaa cgtgacctac 720  
 cctctcagg tgatggcaaa agttctctc acggagggaa gagaattcct aatggaaaag 780

10

atacaggagg ttgtaacaga gcgagaaagg atgtacgacg aatgaagaa aatagaagga 840  
 gttgaggttt ttccgagtaa ggctaacttc ttgcttttca gaacgcctta ccccgcccac 900  
 gaggtttatc aggagctact gaaaagggat gtccctcgta ggaacgtatc ttacatggaa 960  
 ggactccaaa agtgcctcag ggtaagcgta gggaaaccgg aagaaaacaa caagttttctg 1020  
 gaagcactgg aggagagtat aaaatccctt tcaagctctc tttaa 1065

<210> 24  
 <211> 912  
 <212> DNA  
 <213> *Pyrobaculum aerophilum*

<400> 24  
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 aaaatacacg tgttgactca cgcgcttoac tacggaaact ctatattcga gggaaataaga 120  
 gggatttggg acggcgataa tttgctcgta tttaggttag aagaacacat cgacgcgatg 180  
 tacagatcgg ctaagatact aggcataaat attccgtata caagagagga agtccgccaa 240  
 gctgtactag agaccataaa ggctaataac ttccgagagg atgtctacat aagacctgtg 300  
 gcgtttgtcg cctcgcagac ggtgacgctt gacataagaa atttggaagt ctccctcgcg 360  
 gttattgtat tcccatttgg caaatacctc tcgcccacg gcattaagge aacgattgta 420  
 agctggcgta gagtacataa tacaatgctc cctgtgatgg caaaaatcgg cggatatat 480  
 gtaaacctctg tacttgcgct tgtagaggct agaagcaggg gatttgacga ggctttatta 540  
 atggacgtta acggttatgt tgttgagggt tctggagaga atattttcat tgtcagaggt 600  
 ggaaggcttt tcacgcgcgc agtacacgaa tctatcctcg aggggaattac gagggatacg 660  
 gtaataaagc tcagcgggga tgtgggactt cgggtggagg aaaagcctat tacgaggag 720  
 gaggtgtata cagccgacga ggtgttttta gtaggaaccg ccgcagagat aacgccagt 780  
 gtggaggttg acggcagaa aatcggcaca ggcaagccgg gccccattac gacaaaaata 840  
 gctgagctgt actcaaactg cgtgagaggc aaagtagaga aatacttaaa ttggatcact 900  
 cctgtgtatt ag 912

<210> 25  
 <211> 414  
 <212> PRT  
 <213> *Aquifex*

<400> 25

Met Ile Glu Asp Pro M t Asp Trp Ala Phe Pro Arg Ile Lys Arg Leu  
 1 5 10 15

11

Pro Glu Tyr Val Phe Ser Leu Val Asn Glu Leu Lys Tyr Lys Leu Arg  
 20 25 30  
 Arg Glu Gly Glu Asp Val Val Asp Leu Gly Met Gly Asn Pro Asn Met  
 35 40 45  
 Pro Pro Ala Lys His Ile Ile Asp Lys Leu Cys Glu Val Ala Gln Lys  
 50 55 60  
 Pro Asn Val His Gly Tyr Ser Ala Ser Arg Gly Ile Pro Arg Leu Arg  
 65 70 75 80  
 Lys Ala Ile Cys Asn Phe Tyr Glu Glu Arg Tyr Gly Val Lys Leu Asp  
 85 90 95  
 Pro Glu Arg Glu Ala Ile Leu Thr Ile Gly Ala Lys Glu Gly Tyr Ser  
 100 105 110  
 His Leu Met Leu Ala Met Ile Ser Pro Gly Asp Thr Val Ile Val Pro  
 115 120 125  
 Asn Pro Thr Tyr Pro Ile His Tyr Tyr Ala Pro Ile Ile Ala Gly Gly  
 130 135 140  
 Glu Val His Ser Ile Pro Leu Asn Phe Ser Asp Asp Gln Asp His Gln  
 145 150 155 160  
 Glu Glu Phe Leu Arg Arg Leu Tyr Glu Ile Val Lys Thr Ala Met Pro  
 165 170 175  
 Lys Pro Lys Ala Val Val Ile Ser Phe Pro His Asn Pro Thr Thr Ile  
 180 185 190  
 Thr Val Glu Lys Asp Phe Phe Lys Glu Ile Val Lys Phe Ala Lys Glu  
 195 200 205  
 His Gly Leu Trp Ile Ile His Asp Phe Ala Tyr Ala Asp Ile Ala Phe  
 210 215 220  
 Asp Gly Tyr Lys Pro Pro Ser Ile Leu Glu Ile Glu Gly Ala Lys Asp  
 225 230 235 240  
 Val Ala Val Glu Leu Tyr Ser Met Ser Lys Gly Phe Ser Met Ala Gly  
 245 250 255  
 Trp Arg Val Ala Phe Val Val Gly Asn Glu Ile Leu Ile Lys Asn Leu  
 260 265 270  
 Ala His Leu Lys Ser Tyr Leu Asp Tyr Gly Ile Phe Thr Pro Ile Gln  
 275 280 285  
 Val Ala Ser Ile Ile Ala Leu Glu Ser Pro Tyr Glu Ile Val Glu Lys  
 290 295 300  
 Thr Ala Lys Val Tyr Gln Lys Arg Arg Asp Val Leu Val Glu Gly Leu  
 305 310 315 320  
 Asn Arg Leu Gly Trp Lys Val Lys Lys Pro Lys Ala Thr Met Phe Val  
 325 330 335  
 Trp Ala Lys Ile Pro Glu Trp Ile Asn Met Asn Ser Leu Asp Phe Ser

12

340                      345                      350  
 Leu Phe Leu Leu Lys Glu Ala Lys Val Ala Val Ser Pr Gly Val Gly  
       355                      360                      365  
 Phe Gly Gln Tyr Gly Glu Gly Tyr Val Arg Phe Ala Leu Val Glu Asn  
       370                      375                      380  
 Glu His Arg Ile Arg Gln Ala Ile Arg Gly Ile Arg Lys Ala Phe Arg  
       385                      390                      395                      400  
 Lys Leu Gln Lys Glu Arg Lys Leu Glu Pro Glu Arg Ser Ala  
           405                      410  
  
 <210> 26  
 <211> 373  
 <212> PRT  
 <213> Aquifex  
  
 <400> 26  
  
 Met Asp Arg Leu Glu Lys Val Ser Pro Phe Ile Val Met Asp Ile Leu  
  1                      5                      10                      15  
 Ala Gln Ala Gln Lys Tyr Glu Asp Val Val His Met Glu Ile Gly Glu  
           20                      25                      30  
 Pro Asp Leu Glu Pro Ser Pro Lys Val Met Glu Ala Leu Glu Arg Ala  
       35                      40                      45  
 Val Lys Glu Lys Thr Phe Phe Tyr Thr Pro Ala Leu Gly Leu Trp Glu  
       50                      55                      60  
 Leu Arg Glu Arg Ile Ser Glu Phe Tyr Arg Lys Lys Tyr Ser Val Glu  
  65                      70                      75                      80  
 Val Ser Pro Glu Arg Val Ile Val Thr Thr Gly Thr Ser Gly Ala Phe  
           85                      90                      95  
  
 Leu Val Ala Tyr Ala Val Thr Leu Asn Ala Gly Glu Lys Ile Ile Leu  
           100                      105                      110  
 Pro Asp Pro Ser Tyr Pro Cys Tyr Lys Asn Phe Ala Tyr Leu Leu Asp  
       115                      120                      125  
 Ala Gln Pro Val Phe Val Asn Val Asp Lys Glu Thr Asn Tyr Glu Val  
       130                      135                      140  
 Arg Lys Glu Met Ile Glu Asp Ile Asp Ala Lys Ala Leu His Ile Ser  
  145                      150                      155                      160  
 Ser Pro Gln Asn Pro Thr Gly Thr Leu Tyr Ser Pro Glu Thr Leu Lys  
           165                      170                      175  
 Glu Leu Ala Glu Tyr Cys Glu Glu Lys Gly Met Tyr Phe Ile Ser Asp  
       180                      185                      190  
 Glu Ile Tyr His Gly Leu Val Tyr Glu Gly Arg Glu His Thr Ala Leu  
       195                      200                      205  
 Glu Phe Ser Asp Arg Ala Ile Val Ile Asn Gly Phe Ser Lys Tyr Phe

13

210                      215                      220  
 Cys Met Pro Gly Phe Arg Ile Gly Trp Met Ile Val Pr Glu Glu Leu  
 225                      230                      235                      240  
 Val Arg Lys Ala Glu Ile Val Ile Gln Asn Val Phe Ile Ser Ala Pro  
 245                      250                      255  
 Thr Leu Ser Gln Tyr Ala Ala Leu Glu Ala Phe Asp Tyr Glu Tyr Leu  
 260                      265                      270  
 Glu Lys Val Arg Lys Thr Phe Glu Glu Arg Arg Asn Phe Leu Tyr Gly  
 275                      280                      285  
 Glu Leu Lys Lys Leu Phe Lys Ile Asp Ala Lys Pro Gln Gly Ala Phe  
 290                      295                      300  
 Tyr Val Trp Ala Asn Ile Ser Asp Tyr Ser Thr Asp Ser Tyr Glu Phe  
 305                      310                      315                      320  
 Ala Leu Lys Leu Leu Arg Glu Ala Arg Val Ala Val Thr Pro Gly Val  
 325                      330                      335  
 Asp Phe Gly Lys Asn Lys Thr Lys Glu Tyr Ile Arg Phe Ala Tyr Thr  
 340                      345                      350  
 Arg Lys Ile Glu Glu Leu Lys Glu Gly Val Glu Arg Ile Lys Lys Phe  
 355                      360                      365  
 Leu Glu Lys Leu Ser  
 370

<210> 27  
 <211> 453  
 <212> PRT  
 <213> Aquifex

<400> 27

Met Trp Glu Leu Asp Pro Lys Thr Leu Glu Lys Trp Asp Lys Glu Tyr  
 1                      5                      10                      15  
 Phe Trp His Pro Phe Thr Gln Met Lys Val Tyr Arg Glu Glu Glu Asn  
 20                      25                      30  
 Leu Ile Phe Glu Arg Gly Glu Gly Val Tyr Leu Trp Asp Ile Tyr Gly  
 35                      40                      45  
 Arg Lys Tyr Ile Asp Ala Ile Ser Ser Leu Trp Cys Asn Val His Gly  
 50                      55                      60  
 His Asn His Pro Lys Leu Asn Asn Ala Val Met Lys Gln Leu Cys Lys  
 65                      70                      75                      80  
 Val Ala His Thr Thr Thr Leu Gly Ser Ser Asn Val Pro Ala Ile Leu  
 85                      90                      95  
 Leu Ala Lys Lys Leu Val Glu Ile Ser Pro Glu Gly Leu Asn Lys Val  
 100                      105                      110  
 Phe Tyr Ser Glu Asp Gly Ala Glu Ala Val Glu Ile Ala Ile Lys Met



115	120	125
Ala Tyr His Tyr Trp Lys Asn Lys Gly Val Lys Gly Lys Asn Val Phe 130 135 140		
Ile Thr Leu Ser Glu Ala Tyr His Gly Asp Thr Val Gly Ala Val Ser 145 150 155 160		
Val Gly Gly Ile Glu Leu Phe His Gly Thr Tyr Lys Asp Leu Leu Phe 165 170 175		
Lys Thr Ile Lys Leu Pro Ser Pro Tyr Leu Tyr Cys Lys Glu Lys Tyr 180 185 190		
Gly Glu Leu Cys Pro Glu Cys Thr Ala Asp Leu Leu Lys Gln Leu Glu 195 200 205		
Asp Ile Leu Lys Ser Arg Glu Asp Ile Val Ala Val Ile Met Glu Ala 210 215 220		
Gly Ile Gln Ala Ala Ala Gly Met Leu Pro Phe Pro Pro Gly Phe Leu 225 230 235 240		
Lys Gly Val Arg Glu Leu Thr Lys Lys Tyr Asp Thr Leu Met Ile Val 245 250 255		
Asp Glu Val Ala Thr Gly Phe Gly Arg Thr Gly Thr Met Phe Tyr Cys 260 265 270		
Glu Gln Glu Gly Val Ser Pro Asp Phe Met Cys Leu Gly Lys Gly Ile 275 280 285		
Thr Gly Gly Tyr Leu Pro Leu Ala Ala Thr Leu Thr Thr Asp Glu Val 290 295 300		
Phe Asn Ala Phe Leu Gly Glu Phe Gly Glu Ala Lys His Phe Tyr His 305 310 315 320		
Gly His Thr Tyr Thr Gly Asn Asn Leu Ala Cys Ser Val Ala Leu Ala 325 330 335		
Asn Leu Glu Val Phe Glu Glu Glu Arg Thr Leu Glu Lys Leu Gln Pro 340 345 350		
Lys Ile Lys Leu Leu Lys Glu Arg Leu Gln Glu Phe Trp Glu Leu Lys 355 360 365		
His Val Gly Asp Val Arg Gln Leu Gly Phe Met Ala Gly Ile Glu Leu 370 375 380		
Val Lys Asp Lys Glu Lys Gly Glu Pro Phe Pro Tyr Gly Glu Arg Thr 385 390 395 400		
Gly Phe Lys Val Ala Tyr Lys Cys Arg Glu Lys Gly Val Phe Leu Arg 405 410 415		
Pro Leu Gly Asp Val Met Val Leu Met Met Pro Leu Val Ile Glu Glu 420 425 430		
Asp Glu Met Asn Tyr Val Ile Asp Thr Leu Lys Trp Ala Ile Lys Glu 435 440 445		

15

Leu Glu Lys Glu Val  
450

<210> 28  
<211> 343  
<212> PRT  
<213> Aquifex

<400> 28

Met Thr Tyr Leu Met Asn Asn Tyr Ala Arg Leu Pro Val Lys Phe Val  
1 5 10 15

Arg Gly Lys Gly Val Tyr Leu Tyr Asp Glu Glu Gly Lys Glu Tyr Leu  
20 25 30

Asp Phe Val Ser Gly Ile Gly Val Asn Ser Leu Gly His Ala Tyr Pro  
35 40 45

Lys Leu Thr Glu Ala Leu Lys Glu Gln Val Glu Lys Leu Leu His Val  
50 55 60

Ser Asn Leu Tyr Glu Asn Pro Trp Gln Glu Glu Leu Ala His Lys Leu  
65 70 75 80

Val Lys His Phe Trp Thr Glu Gly Lys Val Phe Phe Ala Asn Ser Gly  
85 90 95

Thr Glu Ser Val Glu Ala Ala Ile Lys Leu Ala Arg Lys Tyr Trp Arg  
100 105 110

Asp Lys Gly Lys Asn Lys Trp Lys Phe Ile Ser Phe Glu Asn Ser Phe  
115 120 125

His Gly Arg Thr Tyr Gly Ser Leu Ser Ala Thr Gly Gln Pro Lys Phe  
130 135 140

His Lys Gly Phe Glu Pro Leu Val Pro Gly Phe Ser Tyr Ala Lys Leu  
145 150 155 160

Asn Asp Ile Asp Ser Val Tyr Lys Leu Leu Asp Glu Glu Thr Ala Gly  
165 170 175

Ile Ile Ile Glu Val Ile Gln Gly Glu Gly Gly Val Asn Glu Ala Ser  
180 185 190

Glu Asp Phe Leu Ser Lys Leu Gln Glu Ile Cys Lys Glu Lys Asp Val  
195 200 205

Leu Leu Ile Ile Asp Glu Val Gln Thr Gly Ile Gly Arg Thr Gly Glu  
210 215 220

Phe Tyr Ala Tyr Gln His Phe Asn Leu Lys Pro Asp Val Ile Ala Leu  
225 230 235 240

Ala Lys Gly Leu Gly Gly Gly Val Pro Ile Gly Ala Ile Leu Ala Arg  
245 250 255

Glu Glu Val Ala Gln Ser Phe Thr Pro Gly Ser His Gly Ser Thr Phe  
260 265 270

16

Gly Gly Asn Pro Leu Ala Cys Arg Ala Gly Thr Val Val Val Asp Glu  
275 280 285

Val Glu Lys Leu Leu Pro His Val Arg Glu Val Gly Asn Tyr Phe Lys  
290 295 300

Glu Lys Leu Lys Glu Leu Gly Lys Gly Lys Val Lys Gly Arg Gly Leu  
305 310 315 320

Met Leu Gly Leu Glu Leu Glu Arg Glu Cys Lys Asp Tyr Val Leu Lys  
325 330 335

Ala Leu Glu Arg Asp Phe Ser  
340

<210> 29

<211> 398

<212> PRT

<213> Ammonifex degensii

<400> 29

Met Arg Lys Leu Ala Glu Arg Ala Gln Lys Leu Ser Pro Ser Pro Thr  
1 5 10 15

Leu Ser Val Asp Thr Lys Ala Lys Glu Leu Leu Arg Gln Gly Glu Arg  
20 25 30

Val Ile Asn Phe Gly Ala Gly Glu Pro Asp Phe Asp Thr Pro Glu His  
35 40 45

Ile Lys Glu Ala Ala Lys Arg Ala Leu Asp Gln Gly Phe Thr Lys Tyr  
50 55 60

Thr Pro Val Ala Gly Ile Leu Pro Leu Arg Glu Ala Ile Cys Glu Lys  
65 70 75 80

Leu Tyr Arg Asp Asn Gln Leu Glu Tyr Ser Pro Asn Glu Ile Val Val  
85 90 95

Ser Cys Gly Ala Lys His Ser Ile Phe Asn Ala Leu Gln Val Leu Leu  
100 105 110

Asp Pro Gly Asp Glu Val Ile Ile Pro Val Pro Tyr Trp Thr Ser Tyr  
115 120 125

Pro Glu Gln Val Lys Leu Ala Gly Gly Val Pro Val Phe Val Pro Thr  
130 135 140

Ser Pro Glu Asn Asp Phe Lys Leu Arg Pro Glu Asp Leu Arg Ala Ala  
145 150 155 160

Val Thr Pro Arg Thr Arg Leu Leu Ile Leu Asn Ser Pro Ala Asn Pro  
165 170 175

Thr Gly Thr Val Tyr Arg Arg Glu Glu Leu Ile Gly Leu Ala Glu Val  
180 185 190

Ala Leu Glu Ala Asp Leu Trp Ile Leu Ser Asp Glu Ile Tyr Glu Lys  
195 200 205

17

Leu 11 Tyr Asp Gly Met Glu His Val Ser Ile Ala Ala Leu Asp Pro  
210 215 220

Glu Val Lys Lys Arg Thr Ile Val Val Asn Gly Val Ser Lys Ala Tyr  
225 230 235 240

Ala Met Thr Gly Trp Arg Ile Gly Tyr Ala Ala Ala Pro Arg Pro Ile  
245 250 255

Ala Gln Ala Met Thr Asn Leu Gln Ser His Ser Thr Ser Asn Pro Thr  
260 265 270

Ser Val Ala Gln Ala Ala Ala Leu Ala Ala Leu Lys Gly Pro Gln Glu  
275 280 285

Pro Val Glu Asn Met Arg Arg Ala Phe Gln Lys Arg Arg Asp Phe Ile  
290 295 300

Trp Gln Tyr Leu Asn Ser Leu Pro Gly Val Arg Cys Pro Lys Pro Leu  
305 310 315 320

Gly Ala Phe Tyr Val Phe Pro Glu Val Glu Arg Ala Phe Gly Pro Pro  
325 330 335

Ser Lys Arg Thr Gly Asn Thr Thr Ala Ser Asp Leu Ala Leu Phe Leu  
340 345 350

Leu Glu Glu Ile Lys Val Ala Thr Val Ala Gly Ala Ala Phe Gly Asp  
355 360 365

Asp Arg Tyr Leu Arg Phe Ser Tyr Ala Leu Arg Leu Glu Asp Ile Glu  
370 375 380

Glu Gly Met Gln Arg Phe Lys Glu Leu Ile Glu Ala Ala Leu  
385 390 395

<210> 30  
<211> 592  
<212> PRT  
<213> Aquifex

<400> 30

Met Cys Gly Ile Val Gly Tyr Val Gly Arg Asp Leu Ala Leu Pro Ile  
1 5 10 15

Val Leu Gly Ala Leu Glu Arg Leu Glu Tyr Arg Gly Tyr Asp Ser Ala  
20 25 30

Gly Val Ala Leu Ile Glu Asp Gly Lys Leu Ile Val Glu Lys Lys Lys  
35 40 45

Gly Lys Ile Arg Glu Leu Val Lys Ala Leu Trp Gly Lys Asp Tyr Lys  
50 55 60

Ala Lys Thr Gly Ile Gly His Thr Arg Trp Ala Thr His Gly Lys Pro  
65 70 75 80

Thr Asp Glu Asn Ala His Pro His Thr Asp Glu Lys Gly Glu Phe Ala  
85 90 95

Val Val His Asn Gly Ile Ile Glu Asn Tyr Leu Glu Leu Lys Glu Glu  
 100 105 110  
 Leu Lys Lys Glu Gly Val Lys Phe Arg Ser Glu Thr Asp Thr Glu Val  
 115 120 125  
 Ile Ala His Leu Ile Ala Lys Asn Tyr Arg Gly Asp Leu Leu Glu Ala  
 130 135 140  
 Val Leu Lys Thr Val Lys Lys Leu Lys Gly Ala Phe Ala Phe Ala Val  
 145 150 155 160  
 Ile Thr Val His Glu Pro Asn Arg Leu Ile Gly Val Lys Gln Gly Ser  
 165 170 175  
 Pro Leu Ile Val Gly Leu Gly Glu Gly Glu Asn Phe Leu Ala Ser Asp  
 180 185 190  
 Ile Pro Ala Ile Leu Pro Tyr Thr Lys Lys Ile Ile Val Leu Asp Asp  
 195 200 205  
 Gly Glu Ile Ala Asp Leu Thr Pro Asp Thr Val Asn Ile Tyr Asn Phe  
 210 215 220  
 Glu Gly Glu Pro Val Ser Lys Glu Val Met Ile Thr Pro Trp Asp Leu  
 225 230 235 240  
 Val Ser Ala Glu Lys Gly Gly Phe Lys His Phe Met Leu Lys Glu Ile  
 245 250 255  
 Tyr Glu Gln Pro Lys Ala Ile Asn Asp Thr Leu Lys Gly Phe Leu Ser  
 260 265 270  
 Thr Glu Asp Ala Ile Pro Phe Lys Leu Lys Asp Phe Arg Arg Val Leu  
 275 280 285  
 Ile Ile Ala Cys Gly Thr Ser Tyr His Ala Gly Phe Val Gly Lys Tyr  
 290 295 300  
 Trp Ile Glu Arg Phe Ala Gly Val Pro Thr Glu Val Ile Tyr Ala Ser  
 305 310 315 320  
 Glu Phe Arg Tyr Ala Asp Val Pro Val Ser Asp Lys Asp Ile Val Ile  
 325 330 335  
 Gly Ile Ser Gln Ser Gly Glu Thr Ala Asp Thr Lys Phe Ala Leu Gln  
 340 345 350  
 Ser Ala Lys Glu Lys Gly Ala Phe Thr Val Gly Leu Val Asn Val Val  
 355 360 365  
 Gly Ser Ala Ile Asp Arg Glu Ser Asp Phe Ser Leu His Thr His Ala  
 370 375 380  
 Gly Pro Glu Ile Gly Val Ala Ala Thr Lys Thr Phe Thr Ala Gln Phe  
 385 390 395 400  
 Thr Ala Leu Tyr Ala Leu Ser Val Arg Glu Ser Glu Glu Arg Glu Asn  
 405 410 415

19

Leu Ile Arg Leu Leu Glu Lys Val Pro Ser L u Val Glu Gln Thr Leu  
420 425 430

Asn Thr Ala Glu Glu Val Glu Lys Val Ala Glu Lys Tyr Met Lys Lys  
435 440 445

Lys Asn Met Leu Tyr Leu Gly Arg Tyr Leu Asn Tyr Pro Ile Ala Leu  
450 455 460

Glu Gly Ala Leu Lys Leu Lys Glu Ile Ser Tyr Ile His Ala Glu Gly  
465 470 475 480

Tyr Pro Ala Gly Glu Met Lys His Gly Pro Ile Ala Leu Ile Asp Glu  
485 490 495

Asn Met Pro Val Val Val Ile Ala Pro Lys Asp Arg Val Tyr Glu Lys  
500 505 510

Ile Leu Ser Asn Val Glu Glu Val Leu Ala Arg Lys Gly Arg Val Ile  
515 520 525

Ser Val Gly Phe Lys Gly Asp Glu Thr Leu Lys Ser Lys Ser Glu Ser  
530 535 540

Val Met Glu Ile Pro Lys Ala Glu Glu Pro Ile Thr Pro Phe Leu Thr  
545 550 555 560

Val Ile Pro Leu Gln Leu Phe Ala Tyr Phe Ile Ala Ser Lys Leu Gly  
565 570 575

Leu Asp Val Asp Gln Pro Arg Asn Leu Ala Lys Thr Val Thr Val Glu  
580 585 590

<210> 31

<211> 354

<212> PRT

<213> Aquifex

<400> 31

Met Ile Pro Gln Arg Ile Lys Glu Leu Glu Ala Tyr Lys Thr Glu Val  
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Thr Pro Ala Ser Val Arg Leu Ser Ser Asn Glu Phe Pro Tyr Asp Phe  
20 25 30

Pro Glu Glu Ile Lys Gln Arg Ala Leu Glu Glu Leu Lys Lys Val Pro  
35 40 45

Leu Asn Lys Tyr Pro Asp Pro Glu Ala Lys Glu Leu Lys Ala Val Leu  
50 55 60

Ala Asp Phe Phe Gly Val Lys Glu Glu Asn Leu Val Leu Gly Asn Gly  
65 70 75 80

Ser Asp Glu Leu Ile Tyr Tyr Leu Ser Ile Ala Ile Gly Glu Leu Tyr  
85 90 95

Ile Pro Val Tyr Ile Pro Val Pro Thr Phe Pro Met Tyr Glu Ile Ser  
100 105 110

20

Ala Lys Val Leu Gly Arg Pro Leu Val Lys Val Gln Leu Asp Glu Asn  
115 120 125

Phe Asp Ile Asp Leu Glu Arg Ser Ile Glu Leu Ile Glu Lys Glu Lys  
130 135 140

Pro Val Leu Gly Tyr Phe Ala Tyr Pro Asn Asn Pro Thr Gly Asn Leu  
145 150 155 160

Phe Ser Arg Gly Lys Ile Glu Glu Ile Arg Asn Arg Gly Val Phe Cys  
165 170 175

Val Ile Asp Glu Ala Tyr Tyr His Tyr Ser Gly Glu Thr Phe Leu Glu  
180 185 190

Asp Ala Leu Lys Arg Glu Asp Thr Val Val Leu Arg Thr Leu Ser Lys  
195 200 205

Ile Gly Met Ala Ser Leu Arg Val Gly Ile Leu Ile Gly Lys Gly Glu  
210 215 220

Ile Val Ser Glu Ile Asn Lys Val Arg Leu Pro Phe Asn Val Thr Tyr  
225 230 235 240

Pro Ser Gln Val Met Ala Lys Val Leu Leu Thr Glu Gly Arg Glu Phe  
245 250 255

Leu Met Glu Lys Ile Gln Glu Val Val Thr Glu Arg Glu Arg Met Tyr  
260 265 270

Asp Glu Met Lys Lys Ile Glu Gly Val Glu Val Phe Pro Ser Lys Ala  
275 280 285

Asn Phe Leu Leu Phe Arg Thr Pro Tyr Pro Ala His Glu Val Tyr Gln  
290 295 300

Glu Leu Leu Lys Arg Asp Val Leu Val Arg Asn Val Ser Tyr Met Glu  
305 310 315 320

Gly Leu Gln Lys Cys Leu Arg Val Ser Val Gly Lys Pro Glu Glu Asn  
325 330 335

Asn Lys Phe Leu Glu Ala Leu Glu Glu Ser Ile Lys Ser Leu Ser Ser  
340 345 350

Ser Leu

<210> 32  
<211> 303  
<212> PRT

<213> Pyrobaculum aerophilum  
<400> 32

Met Lys Pro Tyr Ala Lys Tyr Ile Trp Leu Asp Gly Arg Ile Leu Lys  
1 5 10 15

Trp Glu Asp Ala Lys Ile His Val Leu Thr His Ala Leu His Tyr Gly  
20 25 30

21

Thr Ser Ile Phe Glu Gly Ile Arg Gly Tyr Trp Asn Gly Asp Asn Leu  
 35 40 45  
 Leu Val Phe Arg Leu Glu Glu His Ile Asp Arg Met Tyr Arg Ser Ala  
 50 55 60  
 Lys Ile Leu Gly Ile Asn Ile Pro Tyr Thr Arg Glu Glu Val Arg Gln  
 65 70 75 80  
 Ala Val Leu Glu Thr Ile Lys Ala Asn Asn Phe Arg Glu Asp Val Tyr  
 85 90 95  
 Ile Arg Pro Val Ala Phe Val Ala Ser Gln Thr Val Thr Leu Asp Ile  
 100 105 110  
 Arg Asn Leu Glu Val Ser Leu Ala Val Ile Val Phe Pro Phe Gly Lys  
 115 120 125  
 Tyr Leu Ser Pro Asn Gly Ile Lys Ala Thr Ile Val Ser Trp Arg Arg  
 130 135 140  
 Val His Asn Thr Met Leu Pro Val Met Ala Lys Ile Gly Gly Ile Tyr  
 145 150 155 160  
 Val Asn Ser Val Leu Ala Leu Val Glu Ala Arg Ser Arg Gly Phe Asp  
 165 170 175  
 Glu Ala Leu Leu Met Asp Val Asn Gly Tyr Val Val Glu Gly Ser Gly  
 180 185 190  
 Glu Asn Ile Phe Ile Val Arg Gly Gly Arg Leu Phe Thr Pro Pro Val  
 195 200 205  
 His Glu Ser Ile Leu Glu Gly Ile Thr Arg Asp Thr Val Ile Lys Leu  
 210 215 220  
 Ser Gly Asp Val Gly Leu Arg Val Glu Glu Lys Pro Ile Thr Arg Glu  
 225 230 235 240  
 Glu Val Tyr Thr Ala Asp Glu Val Phe Leu Val Gly Thr Ala Ala Glu  
 245 250 255  
 Ile Thr Pro Val Val Glu Val Asp Gly Arg Thr Ile Gly Thr Gly Lys  
 260 265 270  
 Pro Gly Pro Ile Thr Thr Lys Ile Ala Glu Leu Tyr Ser Asn Val Val  
 275 280 285  
 Arg Gly Lys Val Glu Lys Tyr Leu Asn Trp Ile Thr Pro Val Tyr  
 290 295 300

<210> 33  
 <211> 52  
 <212> DNA  
 <213> Artificial sequence

<220>  
 <223> Primer for PCR

<400> 33  
 ccgagaattc attaaagagg agaaattaac tatggcagtc aaagtgcggc ct

52



22

<210> 34  
 <211> 31  
 <212> DNA  
 <213> Artificial sequence

<220>  
 <221> Primer for PCR

<400> 34  
 gaaggacctt cgaaacctat tcttaggagg c 31

<210> 35  
 <211> 1092  
 <212> DNA  
 <213> Ammonifex degensii

<220>  
 <221> misc\_feature  
 <222> (986)..(987)  
 <223> n is any nucleotide

<400> 35  
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 atcgaagagg taaagaagga gctggggctg gaggaggtag tcaagctggc ctccaacgag 120  
 aacctcttgg gacottctcc caaggccgtg gcggcgctgg agggactgga ccaactggcac 180  
 ctttaccag aaggctcaag ctatgagcta cggcaggcgc tgggtaagaa actggagata 240  
 gaccgcgaca gcatcatcgt gggttgoggc tcaagcgaag tcatccagat gctctctttg 300  
 gccctgctgg cggccggcga cgaggtggtc atccctgtgc ctaccttcc ccgctatgag 360  
 cccctggcac ggctcatggg ggctaatacc gtaaaagttc ccttgaagga ctaccgcac 420  
 gatgtggagg cagtggcccg agccctttcc ccccgtaaca agctgggtcta cctatgcaac 480  
 cccaacaacc ccacogggac catcgtcacc cgggaggagg tggagtgggt cttggaaaag 540  
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 gcctaccctg atgggctcga tttcctgcgc cggggctaca atgtggtggt gctgogcacc 660  
 ttctccaaga tctacgggct ggccgggctg cgcatagggt acgggtgtggc ggacagggag 720  
 ctggtggcgg aactgcaccg ggtgogggag cttttcaatg tcagtccgc tgctcagata 780  
 gccgcccctg ccgcocctga agacgaagag ttcggtggcg tttcgcgcca ggtcaacgaa 840  
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 gaggccaact tctactctt cgatgccggt cgggacgagc aggaagtatt tcgocggatg 960  
 ctgcgccagg gagtgatcat ccgggncggg gtgggttata ccaccaactt aagggtgacc 1020  
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23

agggggggttt aa

1092

<210> 36  
 <211> 363  
 <212> PRT  
 <213> Ammonifex degensii  
  
 <220>  
 <221> VARIANT  
  
 <222> (329)..(330)  
 <223> Xaa is any Amino Acid  
  
 <400> 36

Met	Ala	Val	Lys	Val	Arg	Pro	Glu	Leu	Ser	Gln	Val	Glu	Ile	Tyr	Arg
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Pro	Gly	Lys	Pro	Ile	Glu	Glu	Val	Lys	Lys	Glu	Leu	Gly	Leu	Glu	Glu
			20					25					30		
Val	Val	Lys	Leu	Ala	Ser	Asn	Glu	Asn	Pro	Leu	Gly	Pro	Ser	Pro	Lys
		35					40					45			
Ala	Val	Ala	Ala	Leu	Glu	Gly	Leu	Asp	His	Trp	His	Leu	Tyr	Pro	Glu
	50					55					60				
Gly	Ser	Ser	Tyr	Glu	Leu	Arg	Gln	Ala	Leu	Gly	Lys	Lys	Leu	Glu	Ile
65				70						75				80	
Asp	Pro	Asp	Ser	Ile	Ile	Val	Gly	Cys	Gly	Ser	Ser	Glu	Val	Ile	Gln
			85						90					95	
Met	Leu	Ser	Leu	Ala	Leu	Leu	Ala	Pro	Gly	Asp	Glu	Val	Val	Ile	Pro
			100					105					110		
Val	Pro	Thr	Phe	Pro	Arg	Tyr	Glu	Pro	Leu	Ala	Arg	Leu	Met	Gly	Ala
		115					120					125			
Asn	Pro	Val	Lys	Val	Pro	Leu	Lys	Asp	Tyr	Arg	Ile	Asp	Val	Glu	Ala
	130					135					140				
Val	Ala	Arg	Ala	Leu	Ser	Pro	Arg	Thr	Lys	Leu	Val	Tyr	Leu	Cys	Asn
145					150					155				160	
Pro	Asn	Asn	Pro	Thr	Gly	Thr	Ile	Val	Thr	Arg	Glu	Glu	Val	Glu	Trp
			165						170					175	
Phe	Leu	Glu	Lys	Ala	Gly	Glu	Gly	Val	Leu	Thr	Val	Leu	Asp	Glu	Ala
		180					185					190			
Tyr	Cys	Glu	Tyr	Val	Thr	Ser	Pro	Ala	Tyr	Pro	Asp	Gly	Leu	Asp	Phe
	195					200					205				
L u	Arg	Arg	Gly	Tyr	Asn	Val	Val	Val	Leu	Arg	Thr	Phe	Ser	Lys	Ile
	210				215						220				
Tyr	Gly	Leu	Ala	Gly	Leu	Arg	Ile	Gly	Tyr	Gly	Val	Ala	Asp	Arg	Glu
225					230					235					240

24

Leu Val Ala Glu Leu His Arg Val Arg Glu Pro Phe Asn Val Ser Ser  
245 250 255

Ala Ala Gln Ile Ala Ala Leu Ala Ala Leu Glu Asp Glu Glu Phe Val  
260 265 270

Ala Leu Ser Arg Gln Val Asn Glu Glu Gly Lys Val Phe Leu Tyr Arg  
275 280 285

Glu Leu Glu Arg Arg Gly Ile Ala Tyr Val Pro Thr Glu Ala Asn Phe  
290 295 300

Leu Leu Phe Asp Ala Gly Arg Asp Glu Gln Glu Val Phe Arg Arg Met  
305 310 315 320

Leu Arg Gln Gly Val Ile Ile Arg Xaa Gly Val Gly Tyr Pro Thr His  
325 330 335

Leu Arg Val Thr Ile Gly Thr Leu Glu Gln Asn Gln Arg Phe Leu Glu  
340 345 350

Ala Leu Asp Lys Ala Leu Glu Leu Arg Gly Val  
355 360

<210> 37  
<211> 52  
<212> DNA  
<213> Artificial sequence

<220>  
<223> Primer for PCR

<400> 37  
ccgagaattc attaaagagg agaaattaac tatgagaaaa ggacttgcaa gt 52

<210> 38  
<211> 31  
<212> DNA  
<213> Artificial sequence

<220>  
<223> Primer for PCR

<400> 38  
tttcgggaac ttctotagat tcctaggagg c 31

<210> 39  
<211> 1185  
<212> DNA  
<213> Aquifex

<400> 39  
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accgcaaaag caaaagaatt aagggtctaaa ggagtggacg ttatagggtt tggagcggga 120  
gaacctgact tcgacacacc cgacttcata aaggaagcct gtataagggc tttaaggga 180

25

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ggaaagacca agtacgctcc ctccgoggga ataccagagc tcagagaagc tatagctgaa 240
aaactactga aagaaaacaa agttgagtac aaacottcag agatagtcgt ttccgcagga 300
gcgaaaatgg ttctcttccct catattcatg gctatactgg acgaaggaga cgagggtttta 360
ctacctagcc cttactgggt aacttaccoc gaacagataa gggttttcgg aggggttccc 420
gttgagggtc ctctaaagaa agagaaaagga tttcaattaa gtctggaaga tgtgaaagaa 480
aaggttacgg agagaacaaa agctatagtc ataaaotctc cgaacaaccc cactgggtgct 540
gtttacgaag aggaggaact taagaaaata gcggaggtttt gctgggagag gggcattttc 600
ataatttccg atgagtgcct tgagttacttc gtttacgggtg atgcaaaatt tgttagccct 660
gcctctttct cggatgaagt aaagaacata accttcacgg taaacgcctt ttcgaagagc 720
tattccatga ctgggtggcg aatagggttat gtagcgtgac ccgaagagta cgcaaaagtg 780
atagcgagtc ttaacagcca gagtgtttcc aacgtcacta cctttgcccc gtatggagct 840
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aaaccogaag gtgcctttta catatttccg gactttctcc cttacgctga gaaactgggt 1020
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tcggccttcg gagctcccg atttttgagg cttttctacg ccctttccga ggaaagactc 1140
gttgagggtg taaggagaat aaagaaagcc cttgaagaga totaa 1185

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<210> 40  
 <211> 394  
 <212> PRT  
 <213> Aquifex

<400> 40

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Met Arg Lys Gly Leu Ala Ser Arg Val Ser His Leu Lys Pro Ser Pro
1          5          10          15
Thr Leu Thr Ile Thr Ala Lys Ala Lys Glu Leu Arg Ala Lys Gly Val
20          25          30
Asp Val Ile Gly Phe Gly Ala Gly Glu Pro Asp Phe Asp Thr Pro Asp
35          40          45
Phe Ile Lys Glu Ala Cys Ile Arg Ala Leu Arg Glu Gly Lys Thr Lys
50          55          60
Tyr Ala Pro Ser Ala Gly Ile Pro Glu Leu Arg Glu Ala Ile Ala Glu
65          70          75          80
Lys Leu Leu Lys Glu Asn Lys Val Glu Tyr Lys Pro Ser Glu Ile Val
85          90          95
Val Ser Ala Gly Ala Lys Met Val Leu Phe Leu Ile Phe Met Ala Ile

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26

100 105 110  
 Leu Asp Glu Gly Asp Glu Val Leu Leu Pro Ser Pro Tyr Trp Val Thr  
 115 120 125  
 Tyr Pro Glu Gln Ile Arg Phe Phe Gly Gly Val Pro Val Glu Val Pro  
 130 135 140  
 Leu Lys Lys Glu Lys Gly Phe Gln Leu Ser Leu Glu Asp Val Lys Glu  
 145 150 155 160  
 Lys Val Thr Glu Arg Thr Lys Ala Ile Val Ile Asn Ser Pro Asn Asn  
 165 170 175  
 Pro Thr Gly Ala Val Tyr Glu Glu Glu Glu Leu Lys Lys Ile Ala Glu  
 180 185 190  
 Phe Cys Val Glu Arg Gly Ile Phe Ile Ile Ser Asp Glu Cys Tyr Glu  
 195 200 205  
 Tyr Phe Val Tyr Gly Asp Ala Lys Phe Val Ser Pro Ala Ser Phe Ser  
 210 215 220  
 Asp Glu Val Lys Asn Ile Thr Phe Thr Val Asn Ala Phe Ser Lys Ser  
 225 230 235 240  
 Tyr Ser Met Thr Gly Trp Arg Ile Gly Tyr Val Ala Cys Pro Glu Glu  
 245 250 255  
 Tyr Ala Lys Val Ile Ala Ser Leu Asn Ser Gln Ser Val Ser Asn Val  
 260 265 270  
 Thr Thr Phe Ala Gln Tyr Gly Ala Leu Glu Ala Leu Lys Asn Pro Lys  
 275 280 285  
 Ser Lys Asp Phe Val Asn Glu Met Arg Asn Ala Phe Glu Arg Arg Arg  
 290 295 300  
 Asp Thr Ala Val Glu Glu Leu Ser Lys Ile Pro Gly Met Asp Val Val  
 305 310 315 320  
 Lys Pro Glu Gly Ala Phe Tyr Ile Phe Pro Asp Phe Ser Ala Tyr Ala  
 325 330 335  
 Glu Lys Leu Gly Gly Asp Val Lys Leu Ser Glu Phe Leu Leu Glu Lys  
 340 345 350  
 Ala Lys Val Ala Val Val Pro Gly Ser Ala Phe Gly Ala Pro Gly Phe  
 355 360 365  
 Leu Arg Leu Ser Tyr Ala Leu Ser Glu Glu Arg Leu Val Glu Gly Ile  
 370 375 380  
 Arg Arg Ile Lys Lys Ala Leu Glu Glu Ile  
 385 390